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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,079	10/02/2003	Iris Pecker	26871	7751

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,079	PECKER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4 are pending and are currently being examined.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Inventor Friedmann has not initialed and dated the changes in residence and post office address.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,664,105 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims 1-3 encompasses the antisense oligonucleotide comprising a polynucleotide that targets and inhibits the expression (i.e., mRNA) of the heparanase polynucleotides recited in the '105 claims. The "sense" nucleic acid molecule sequence is contained in the anti-sense sequence claimed in the '105 claims.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at thetime of invention of the claimed oligonucleotide comprising a nucleic acid sequence specifically hybridizable with heparanase encoding nucleic acid, an antisense nucleic acid molecule comprising a nucleic acid sequence specifically hybridizable with heparanase messenger RNA, a sense nucleic acid molecule comprising a nucleic acid sequence specifically hybridizable with heparanase antisense RNA, nor a pair of PCR primers comprising a sense primer and an antisense primer, each of said primers including a nucleic acid sequence specifically hybridizable with heparanase encoding nucleic acid.

The instant claims nucleic acid molecules encoding or hybridizing, to some undisclosed degree, with those nucleic acid molecules encoding heparanases of undisclosed structure. There is insufficient disclosure in the specification for said antibodies.

The specification discloses that the cloning and expression of human heparanase gene are described in US Patent No. 5,968,822 (page 4 at lines 13-16). The specification further discloses that the protein product of the said human gene is 61-63kDa (page 4 at lines 25-28 and page 5 at lines 25-28), and that heparanase activity was measured as the ability to degrade HS. The specification discloses that the heparanase nucleic acid is SEQ ID NO: 1 and 3 (page 27 at lines 10-13) and that SEQ ID NO: 4 and 5 are sense and antisense primers, respectively for SEQ ID NO: 1 and 3 (page 27 at lines 16-20) and that total RNA in various cell types was reverse transcribed and amplified using the cDNA primers SEQ ID NO: 6 and 7 (page 30 at lines 10-13).

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as nucleic acid molecules encoding or complementary to or hybridizable with "heparanase" or a portion thereof, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of having heparanase activity. It does not specifically define any of the compounds that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. In addition, a definition by function and in the instant case by the activity and wherein the said activity is not correlated with a specific structural feature, does not suffice to define the genus because it is only an indication of what the property the heparanase has, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

8. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how make and or/use claimed oligonucleotide comprising a nucleic acid sequence specifically hybridizable with heparanase encoding nucleic acid, an antisense nucleic acid molecule comprising a nucleic acid sequence specifically hybridizable with heparanase messenger RNA, a sense nucleic acid molecule comprising a nucleic acid sequence specifically hybridizable with heparanase antisense RNA, nor a pair of PCR primers comprising a sense primer and an antisense primer, each of said primers including a nucleic acid sequence specifically hybridizable with heparanase encoding nucleic acid. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass nucleic acid molecules encoding proteins or portions thereof of heparanases

of undisclosed structure or those nucleic acid molecules specifically hybridizable with heparanase encoding nucleic acid molecules, sense or antisense molecules. There is insufficient disclosure in the specification for said nucleic acid molecules.

The specification discloses that the cloning and expression of human heparanase gene are described in US Patent No. 5,968,822 (page 4 at lines 13-16). The specification further discloses that the protein product of the said human gene is 61-63kDa (page 4 at lines 25-28 and page 5 at lines 25-28), and that heparanase activity was measured as the ability to degrade HS. The specification discloses that the heparanase nucleic acid is SEQ ID NO: 1 and 3 (page 27 at lines 10-13) and that SEQ ID NO: 4 and 5 are sense and antisense primers, respectively for SEQ ID NO: 1 and 3 (page 27 at lines 16-20) and that total RNA in various cell types was reverse transcribed and amplified using the cDNA primers SEQ ID NO: 6 and 7 (page 30 at lines 10-13).

The specification further discloses heparanases possessing widely disparate amino acid sequences, for example those cited on page 8 at lines 16-18 of the instant application, i.e., mouse B16-10 heparanase, human platelet heparanase, heparanases produced by several human tumor cell lines and CHO cells.

The specification does not disclose the conditions that define the recited limitation "specifically hybridizable" with the nucleic acid molecules recited in the instant claims.

In addition, there is no disclosure in the instant specification as to which amino acid residues at which positions comprise heparanase binding sites, which amino acid residues at other positions are tolerant of allowing the heparanase binding sites to function.

The predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain function and properties requires a knowledge of, and guidance with regard to which amino acid residues at which positions in the amino acid sequence, if any are tolerant to modification and which are intolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its function. Evidentiary reference Ngo et al (The Protein Folding Problem and Tertiary Structure Prediction, Merz & LeGrand, Birkhauser Boston, pages 491-495, 1994, entire article, especially Section 6, paragraph 1) teaches that the relationship between the sequence of a peptide and its tertiary structure (i.e., its activity) are not well understood and are therefore not predictable.

Because of this lack of guidance and the extended experimentation that would be required to determine which sequences and/or substitutions would be acceptable to produce/or retain functional activity, it would require undue experimentation for one of skill in the art to arrive at amino acid sequences that would have functional activity, and hence the nucleic acid molecules that encode them or are specifically hybridizable to them. In addition, in Amgen v. Chugai, 18 USPQ 2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with

a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 U.S.C. 112, first paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required on one of skill in the art for the determination of other nucleic acid sequences that are embraced by the claim. This is the situation under consideration. In other words, since it would require undue experimentation to identify amino acid sequences that have functional activity, it would require undue experimentation to make their corresponding nucleic acids.

Undue experimentation would be required of one skilled in the art to make and/or use (including use as a therapeutic agent) the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 are indefinite in the recitation of "specifically hybridizable" because it is not known what is meant. The specification does not disclose the definition of "specifically hybridizable".

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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